**Nicole Putnam, Ph.D., of Vanderbilt University**   
[**“The impact of innate immune recognition of Staphylococcus aureus on bone homeostasis and skeletal immunity”**](https://www.niaid.nih.gov/sites/default/files/nicoleputnamapplicationF31.pdf)

**Description of Institutional Environment and Commitment to Training:**

###### DESCRIPTION OF INSTITUTIONAL ENVIRONMENT AND COMMITMENT TO TRAINING

**Institutional Environment**

Vanderbilt University has outstanding institutional resources and shared core facilities, providing an ideal environment for the completion of the proposed Research Strategy. Through the coordinated actions of the Biomedical Research, Education, and Training (BRET) office, Vanderbilt University displays a strong commitment to graduate students and post-doctoral fellows by providing resources such as career development, the ASPIRE program, Responsible Conduct of Research training, poster-printing services, and additional training programs.

###### Departmental Environment

Commitment to the training of students is also robust at the departmental level. The Department of Pathology, Microbiology, and Immunology (PMI) has faculty members that are heavily involved in the training of students in the Graduate Program in Microbiology and Immunology (M&I), through training at the classroom level and through sustained interactions with graduate students at research seminars and journal clubs. This graduate program benefits immensely by being housed within the larger department of PMI, with close access to resources, seminars, and expertise available from the Vanderbilt Center for Microbial Pathogenesis (VCMP) and the Vanderbilt Center for Immunobiology (VCI).

###### Proposed Development Plan

My research proposal is at the crossroads of microbial pathogenesis, immunology, and bone biology. These areas are well-represented on my Ph.D. Committee through PMI faculty members and physicians. This research is supported by Directors of VCMP and VCI, and investigators affiliated with the Vanderbilt Center for Bone Biology (VCBB) and the Vanderbilt University Institute for Imaging Sciences (VUIIS). Furthermore, there are a number of investigators at Vanderbilt University conducting research complementary to the work detailed in this proposal, including:

* Dr. Eric Skaar, Director of the Center for Microbial Pathogenesis, PMI faculty: Heme iron nutrient utilization in staphylococcal pathogenesis (complementary to Aims 1 and 2)
* Dr. Jeff Rathmell, Director of the Center for Immunobiology, PMI faculty: Mechanisms by which metabolism modulates inflammatory diseases (complementary to Aims 1 and 2)
* Dr. Dan Moore, Vanderbilt Children’s Hospital, PMI faculty: Mechanisms of immune tolerance and immune-mediated tissue injury in autoimmunity (complementary to Aims 1 and 2)
* Dr. Isaac Thomsen, Vanderbilt Children’s Hospital: Serologic responses to toxins during osteomyelitis and other invasive *S. aureus* infections (complementary to Aim 2)
* Dr. Dan Perrien, VUIIS, VCBB: Fracture repair, distraction osteogenesis, and bone remodeling (complementary to Aim 2)
* Dr. Rachelle Johnson, VCBB: Hypoxic regulation of cancer metastases in bone (complementary to Aim 2)
* Dr. Scott Guelcher, VCBB: Local drug delivery in bone fractures complicated by invasive *S. aureus*

infection (complementary to Aim 2)

###### Intellectual Environment

After reaching candidacy, the student’s remaining time in the Ph.D. program is dedicated primarily to research and participation in seminars and journal clubs. Students are required to give two lectures on their research in the M&I Research in Progress weekly seminar series attended by students, postdoctoral fellows, and faculty, which I will be presenting in the spring of 2017 and spring of 2019. Additionally, the Microbial-Host Interaction bi-monthly meeting supports presentation of research to graduate students before their third year and on a more regular basis; I was able to share my research in the spring of 2016 and will again present in January 2017. M&I also supports a bi-monthly journal club run by students, focusing on microbial pathogen- host interactions. In this journal club, I presented a manuscript in 2015 from the laboratory of Gabriel Nunez, to introduce his work prior to his visit to Vanderbilt later that month. Furthermore, VCBB holds weekly seminars for Vanderbilt students, faculty, and physicians across departments and disciplines with the common theme of studying bone-related research or disease. These seminars and journal clubs create venues for the productive interaction between students, postdoctoral fellows, faculty members, and physicians on a scholarly level to discuss student research, published research articles, clinical presentation of disease, or to introduce previous

work from visiting faculty members. In addition to these internal events, there is also a PMI weekly seminar series that boasts both internal and external speakers, a monthly Inflammation, Infection, and Immunity Frontiers seminar series that invites distinguished research faculty to Vanderbilt, and an annual Vanderbilt Symposium on Infection and Immunity. Vanderbilt facilitates broad discussions to enhance the intellectual environment through discussions between trainees and faculty through seminars and journal clubs and opportunities to meet with outstanding internal and external speakers.

###### Resources for Proposed Research

Vanderbilt University has an exceptional system of core facilities that I will utilize throughout the completion of my proposed Research Strategy. All proposed research is dependent on primary cell utilization and animal infection models, which is supported by the Division of Animal Care and veterinary care services. Resources for the completion of bone histological techniques and analyses, as well as the ability to render 3- dimensional images and perform quantitative analyses of bone remodeling changes are dependent on the unique and state-of-the-art resources available through the VCBB and VUIIS. Additionally, the VCMP and the Vanderbilt Institute for Clinical and Translational Research (VICTR) have contributed to my training and development of this research proposal. These resources are detailed in the Facilities and Other Resources document.

###### Resources for Career Development

The BRET office facilitates career development opportunities at Vanderbilt University, with Career Connection seminars and an annual BRET Career Symposium, both of which I attended in 2016. My interest in establishing a career as an independent scientific investigator with a focus on clinically-important infectious disease and translational research has been supported by Vanderbilt University on several fronts already. BRET offers training programs, such as the Vanderbilt Program in Molecular Medicine (VPMM), which I was accepted into in 2015 to shadow and receive clinical experience in Pediatric Infectious Diseases with my clinical mentor, Dr. Isaac Thomsen. This program includes tailored coursework, including Introduction to Clinical and Translational Research and VPMM Rounds with physicians, basic researchers, and patients. Moreover, the VPMM offers weekly seminars presented by clinicians, researchers, students, and postdoctoral fellows, Bench-to-Bedside symposia, and opportunities to attend clinical conferences, clinical boards, and clinical research seminars.

Vanderbilt has a remarkable career development program for its students, the ASPIRE Program, developed and funded through the 2013 Broadening Experiences in Scientific Training (BEST) NIH Award. M&I graduate students are encouraged to take advantage of the many offerings of this program during their graduate studies to explore career options through workshops and symposiums and expand skill sets through ASPIRE modules, externships, and internships. Due to my future career interests, I applied and was accepted into the ASPIRE Module on Clinical Laboratory Medicine (Clinical Microbiology) in 2016, which will start in January of 2017.

**Nico Contreras, University of Arizona**

[**“The Immunological Consequences of Mouse Cytomegalovirus on Adipose Tissue”**](https://www.niaid.nih.gov/sites/default/files/F31-sample-application_nico_contreras.pdf)

**Description of Institutional Environment and Commitment to Training:**

#### DESCRIPTION OF INSTITUTIONAL ENVIRONMENT

Nico A. Contreras is situated in an ideal clinical research environment, replete with resources to facilitate training and help him develop into a successful investigator in immunobiology and virology.

The University of Arizona (UA) is the leading public research university in the American Southwest. UA provides an unusually interactive interdisciplinary academic community, highly conducive to the proposed project. UA is a land grant public university and has a 387- acre campus in Tucson, Arizona. The campus includes 159 buildings on the main campus and 25 buildings at the adjacent Health Sciences Center. With close to 40,000 students, 20 Colleges, and over 300 academic programs, the UA provides a rich environment for interacting with students, faculty and researchers from many diverse disciplines. The University’s commitment to research was recognized by its ranking from the National Science Foundation as 19th among public universities in the US for research. The UA is one of 63 members of the prestigious Association of American Universities and has over $625 million in annual research funding.

The university is comprised of 13 colleges, one branch campus in Sierra Vista, and has expanded over the last few years in its colleges of Medicine, Pharmacy and Public Health to downtown Phoenix. The UA also has two supporting colleges—Honors and Outreach—and 76 research centers. More than 345 undergraduate, graduate and professional degree programs are offered on a semester schedule.

Educational programs designed to meet the demand for virtual, hybrid, and distance offerings, are added, coordinated, and managed through the Outreach College. The UA offers a range of courses that cover fundamental and advanced concepts and analytic methods pertaining to the design, analysis and interpretation of research studies. Furthermore, the University of Arizona is strongly committed to diversity, with greater than 25% of graduate and professional students being of an ethnically diverse background.

The University of Arizona’s Department of Immunobiology has a diverse array of faculty members involved in numerous research foci, providing broad and deep technical training on multiple platforms. Research in the department are centered in various areas, including neuroimmunology, adaptive, innate and microbial signaling (cellular and subcellular), autoimmunity, bacteriology, parasitology, aging, and virology. The Department promotes a collaborative environment, bolstered by the open laboratory space design within the Medical Research Building. Further collaboration is encouraged during weekly joint laboratory meetings of the Nikolich- Zugich, Schenten, Frelinger, Kuhns, and Wu laboratories, of which Nico is currently the organizer. Equipment is often shared between multiple laboratories including the flow cytometers, PCR machines, microscopes, and AutoMACS.

The Department also holds weekly joint student seminars with the Department of Cellular and Molecular Medicine to develop cross-disciplinary collaboration and communication. Furthermore, there is a weekly Immunobiology Journal Club that critically discuss current original basic, clinical and health services research articles linked to immunobiology; Nico is also the student organizer for this course. As alluded to in the Sponsor’s Section, the Department holds the annual Frontiers in Immunobiology Symposium and has access to several cross-departmental seminars. Previously invited speakers include Drs. Charles Surh (Immune homeostasis in aging); Michael Diamond (Immunity to flaviviruses with aging), Ellias Haddad (Innate immune defects with aging) and others.

By attending these symposia and seminars, Nico has ample opportunities for intellectual interactions with immunobiologists and scientists with a variety of focuses. Opportunities for intellectual interactions with viologists, biostatisticians, immunologists, and other scientists are also available for Nico at UA and its community.

The University of Arizona’s Department of Immunobiology PhD program is on average a 5-year graduation cycle. Coursework is completed within 1.5 years into the program, with a continuation of Journal Club, Joint Student Seminars, and Departmental Seminars until graduation. The qualifying exam is to be completed by the end of the 2nd year and includes an R01 style grant submission followed by an oral defense using the written submission as a framework for discussion, questions, and future experimental designs. Formal progress is followed by submission of several documents to the University’s online UAccess portal, where committees, announcements, and results are submitted and available.

**Samantha Lynne Schwartz, Emory University**

[**“Regulation of 2'-5'-Oligoadenylate Synthetase 1 (OAS1) by dsRNA”**](http://www.niaid.nih.gov/sites/default/files/F31-Sample-Application_Samantha-Schwartz.pdf)

**Description of Institutional Environment and Commitment to Training:**

### INSTITUTIONAL ENVIRONMENT AND COMMITMENT TO TRAINING

**Samantha Schwartz** is a 2nd-year student (rising 3rd year by time of potential award of this NRSA F31 fellowship) in the interdepartmental Biochemistry, Cell, and Developmental Biology (BCDB) Graduate Program at Emory University. Sam has completed all required core Program coursework to date and passed her written qualifying exam in April 2016. Remaining Program commitments include a biostatistics course and a semester- long teaching assistantship. Both of these obligations will be completed in the Spring 2017 semester prior to an award of this NRSA F31 fellowship. Sam has assembled her thesis committee, comprising Drs. Conn (Sam’s Sponsor on this application), Lowen (Co-sponsor), Christine Dunham, Rick Kahn, and Daniel Reines.

**Technical, Intellectual and Other Supporting Resources at Emory University**. Sam’s research and professional training will benefit from outstanding technical, intellectual, and other resources available directly within the Conn and Lowen laboratories, as well as the Departments of Biochemistry (Conn) and Microbiology & Immunology (Lowen), the Emory School of Medicine and its Core facilities, the BCDB Graduate Program, and the Laney Graduate School (LGS) at Emory University. In terms of equipment and other facilities, both the Sponsor and Co-sponsor labs are well-equipped for the proposed studies. The Conn lab has the equipment and resources needed for modern biochemical and biophysical approaches to study the structures, interactions, and biological functions of biomedically important RNA and protein molecules. Additional shared facilities that Sam will use in her work include the Biochemistry structural biology facility, which contains robotics for automated crystallization screens and an X-ray generator for crystal screening. The Department also supports regular access to the SER-CAT beamlines at APS (see Equipment and Facilities sections for details). The Lowen lab is similarly well-equipped for cell culture and viral infection experiments. Sam will use several of Emory’s excellent core facilities, including the Emory Chemical Biology Discovery Core for their OctetRED384 and the HDX-MS Core. In both cases, Sam will work directly on protocol development, data collection, and analysis on these state-of-the-art instruments under the guidance of expert corestaff.

Sam’s research is centered on understanding how a key component of the human innate immune system (OAS1) is regulated by specific features within double-stranded RNA (dsRNA) molecules. Among labs working today on the OAS1/ RNase L pathway, Sam’s project is unique with its specific focus on understanding the *RNA features* that potently activate OAS1 or that can lead to sequestration of its activity. Sam will extend the Conn lab’s strong record of using RNA biochemistry/structural biology approaches to investigate the regulation of dsRNA sensors of the innate immune system by viral and cellular non-coding RNAs. This project builds directly on that of a former graduate student (Dr. Virginia Vachon) and will complement that of a current BCDB graduate student (Ms. Brenda Calderon) whose project is centered on the cellular structured non-coding RNA nc886. The environments in which Sam will work are also enriched by other PhD and graduate student investigators working on RNA-protein interactions related to bacterial antibiotic resistance (Conn lab) and viral transmission, reassortment, and host immunity (Lowen lab). Outside of the Conn and Lowen labs, Sam will have the opportunity to interact with other faculty members and their teams in both informal and formal settings. For example, Sam’s thesis committee has three additional members in addition to Drs. Conn and Lowen who bring diverse expertise, including translational control and ribosome structural biology (Dunham), RNA biology and protein-RNA interactions related to eukaryotic transcription regulation (Reines), and cell and protein biology (Kahn). Other faculty members in Biochemistry with strong research programs in structural biology include Drs. Eric Ortlund (steroid hormone receptors, including protein-RNA interactions, using X-ray crystallography) and Bo Liang (viral RNA-dependent RNA polymerase structures by high-resolution cryo-EM). Sam will participate in the monthly Joint Structural Biology Groups (JSBG) meeting and the “Emory RNA Club,” which connects researchers with interests in RNA biology from Biochemistry, Biology, Cell Biology, and other departments across campus. More broadly, through her interactions with Dr. Lowen’s lab, Sam will benefit from exposure to the great strengths at Emory in virology and vaccine development.

Sam will have many opportunities to present and receive feedback on her work. She will present research updates at least 3-4 times a year in bi-weekly joint Conn-Dunham and Lowen lab meetings. Sam will meet twice a year with her thesis committee and will present her latest research to faculty and students in the BCDB Advanced Seminar course once per year until graduation. Sam will present her work at the JSBG and RNA Club meetings, as well as at Emory symposia (including the Division Student Advisory Council (DSAC) Annual Research Symposium (sponsored by the LGS)) and other local meetings, such as the Southeastern Regional Virology Conference. The LGS also provides professional development support funds for students to present their work at national and international meetings. Finally, Sam will benefit from a number of innovative approaches the BCDB program has implemented to support student professional development, e.g. by requiring yearly updates to her individual development plan (IDP) and allocating time during thesis committee meetings to discuss her career goals. Sam also has access to career seminars, such as “Pathways Beyond the Professoriate” and professionalization workshops offered by the BCDB program.

### ADDITIONAL EDUCATIONAL INFORMATION

**Program Structure**. The BCDB Program is one of 9 graduate training programs in the Graduate Division of Biological and Biomedical Sciences (GDBBS), part of the LGS of Emory University. The BCDB Program is highly interdisciplinary with ~45 training faculty representing 13 basic science and clinical departments and offering an incredible breadth of potential training. Faculty research is grouped into four overarching themes: Biochemistry/ Structural Biology, Cancer Biology, Cell Biology, and Developmental Biology. The Program has a history of implementing innovative approaches to graduate education that emphasize oral and written communication skills, quantitative skills, career development, and professionalization, along with cutting edge technical research training. Our graduates are expected to have the technical, analytical, and communication skills necessary to pursue an independent career in academic, industrial, or government research or in careers where their training will facilitate the business, application, or public understanding of biomedicalresearch.

**Required Milestones & Timing**. ***(a) Coursework***. The BCDB curriculum is intended to provide students with the basic knowledge and skills to pursue doctoral dissertation research and a career in the disciplines represented by the Program. All required coursework is completed by the end of the Spring semester of Year 2, and electives may be taken starting in Year 2 if desired. *The following core courses are required for all BCDB students*: *Year 1*, Foundations in BCDB I and II (BCDB 501/502), Beginning Seminar (BCDB 570r; including attendance at Advanced Seminar), and Jones Program in Ethics (JPE 600); *Year 2*, Statistical Design and Analysis of Experiments (IBS 538), Hypothesis Design and Scientific Writing (IBS 522r), and, Advanced Seminar (BCDB 790r). Additionally, three 10-week research rotations are completed in Year 1, and in most cases, students then select a thesis advisor (typically in May). ***(b) Teaching commitment***. Formal instruction and experience in teaching is a requirement for all graduate students at Emory. The Teaching Assistant Training and Teaching Opportunity (TATTO) Program is administered by the LGS to provide teacher training, and BCDB Trainees fulfill this requirement in Year 2 by *(i)* participation in a 2-day teaching training workshop (TATT 600) covering methods and ethics of teaching, as well as content-specific practice sessions tailored to the discipline of the student, and *(ii)* serving as a Teaching Assistant (TA) for at least one semester, with the quality of the teaching experience being evaluated via reports from the course directors. Several options are available to BCDB students who wish to gain additional teaching experience and t o establish teaching credentials, subject to continued satisfactory progress in their dissertation research subject. ***(c) Qualifying exams (QE)***. The BCDB QE is completed in two parts. **QE1** (May/June Year 1) is a written (essay- type question), closed-book examination administered over two days. QE1 is designed to test foundational knowledge and critical thinking/writing, and thus student preparedness to progress in the Program. **QE2** (to be completed before June 1 of Year 2) is an oral examination designed to assess the student's ability to integrate different aspects of the first two years of graduate training including lab work, data interpretation, hypothesis development, research design, presentation of research, and all other course work. ***(d) Dissertation defense*.** The BCDB Program requires students to produce a rigorous body of novel research, including at least one first- author peer-reviewed research paper, published or accepted for publication, before the dissertation defense is scheduled. Before the PhD degree will be granted, the following tasks must then be completed in order: *(i)* submission of the written dissertation, *(ii)* a closed session oral examination (defense) by the student’s thesis committee, and *(iii)* an advertised public oral presentation of the thesis research.

**Monitoring and Evaluation of Student Progress**. Student progress is monitored from initial entry into the Program via an established, formal process involving academic probation (based on coursework grades and average semester GPA) and the requirements for its resolution through improved performance. Failure to satisfy these criteria is grounds for termination from the BCDB Program. After completion of QE1 and no later than the Spring semester in Year 2, students must form a Dissertation Committee comprising the dissertation advisor and a minimum of four other faculty members, at least three of whom must be BCDB faculty members. The first committee meeting is held no later than six months after passing QE2, and thereafter meetings are required *every six months* (every *four* months after Year 5)*.* Compliance is tracked by the BCDB Executive Committee. The Program requires the following slides in meeting presentations: *(i)* scientific update: techniques learned, papers, grants, presentations, awards, etc., *(ii)* short-term goals, and *(iii)* goals beyond graduate school. **The average time to PhD degree for BCDB students over the last 10 years is 5.8 years.** Sam is on track to graduate within this timeframe.

#### *Provided by Michael Koval, Ph.D. (BCDB Director) & Graeme L. Conn Ph.D. (BCDB Dir. Grad. Studies)*